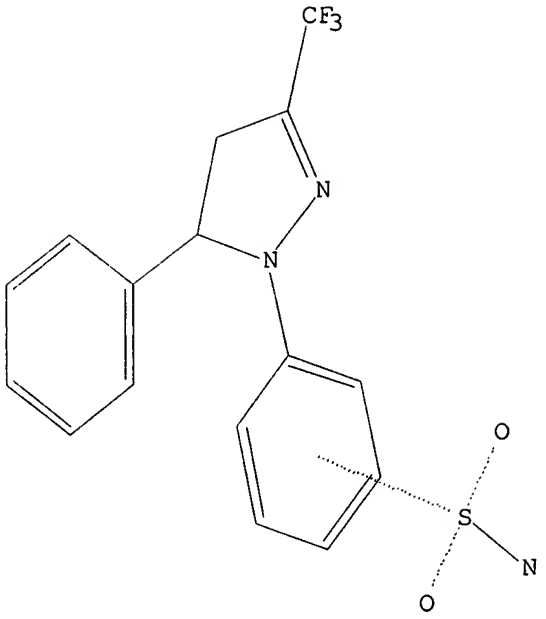

Structure attributes must be viewed using STN Express query preparation.

=> s l5 full
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FULL SCREEN SEARCH COMPLETED - 1576 TO ITERATE

100.0% PROCESSED 1576 ITERATIONS 39 ANSWERS
SEARCH TIME: 00.00.01

L6 39 SEA SSS FUL L5

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	503.46	503.67

FILE 'CAPLUS' ENTERED AT 10:49:15 ON 04 JAN 2006
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FILE COVERS 1907 - 4 Jan 2006 VOL 144 ISS 2

FILE LAST UPDATED: 3 Jan 2006 (20060103/ED)

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=> s l6
L7 12 L6

=> d ibib abs hitstr 1-12

1- instant app

2 - x

3 - x

4 - x

5 - x

6 - x

7 - 103

8 - x

9 - x

10 - x

11 - x

12 - 103

L7 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:823320 CAPLUS
DOCUMENT NUMBER: 143:229840
TITLE: A preparation of pyrazolylbenzenesulfonamide derivatives, useful as antitumor agents
INVENTOR(S): Altisen, Rosa Cuberes; Constansa, Jordi Frigola; Bafalluy, Ramon Mangues; Rigat, Isolda Casanova
PATENT ASSIGNEE(S): Spain
SOURCE: U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

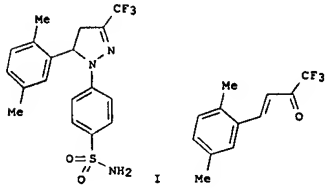
Instant App

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005182119	A1	20050818	US 2004-804695	20040319
ES 2238923	A1	20050901	ES 2004-362	20040216
WO 2005077910	A1	20050825	WO 2005-EP1656	20050216

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: ES 2004-362 A 20040216
US 2004-804695 A 20040319

GI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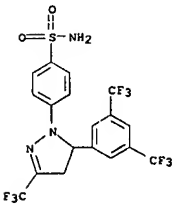
II

L7 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



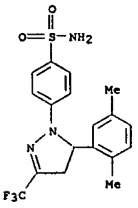
formula I'

L7 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

AB The invention relates to a preparation of pyrazolylbenzenesulfonamide derivs., e.g. I, useful for the treatment of cancer, in particular for the treatment of brain cancer, bone cancer, lip cancer, mouth cancer, esophageal cancer, stomach cancer, liver cancer, bladder cancer, pancreas cancer, ovary cancer, cervical cancer, lung cancer, breast cancer, skin cancer, especially for the treatment of colon cancer and/or bowel cancer and/or prostate cancer. For instance, pyrazolylbenzenesulfonamide derivative I (antitumor activity, IC50 (μM): TD20 - 20.5, NC59 - 16.3; HCA7 - 10.5) was prepared via heterocyclization of (E)-butenone derivative II with 4-aminosulfonylphenylhydrazine hydrochloride.

IT 862536-60-5P 862536-62-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazolylbenzenesulfonamide derivs. useful as antitumor agents)

RN 862536-60-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,5-dimethylphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



formula I

RN 862536-62-7 CAPLUS
CN Benzenesulfonamide, 4-[5-[3,5-bis(trifluoromethyl)phenyl]-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

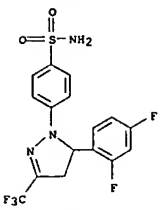
L7 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:365658 CAPLUS
DOCUMENT NUMBER: 140:385445
TITLE: Enantioselective HPLC determination of E-6087, a new COX-2 inhibitor, in human plasma: Validation and pharmacokinetic application
AUTHOR(S): Salgado, Leonardo; Encina, Gregorio; Farran, Ramon; Puig, Santiago; Martinez, Luis
CORPORATE SOURCE: Laboratorios Dr. Esteve, Pharmacokinetics and Drug Metabolism Department, Barcelona, Spain
SOURCE: Chirality (2004), 16(5), 302-308
CODEN: CHRLEP; ISSN: 0899-0042
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB E-6087 is a nonsteroidal anti-inflammatory compound that selectively inhibits cyclooxygenase-2. Because E-6087 has a chiral center, this compound is a racemic mixture of two stereoisomers, (+)-(R)-E-6087 (E-6231) and (-)-(S)-E-6087 (E-6232). A normal-phase liquid-chromatog. method for the enantioselective determination of E-6087 in human plasma was developed and validated. The samples were extracted using solid-phase extraction cartridges containing C18 sorbent, and the exts. were redissolved in absolute ethanol and injected into the chromatog. system. The enantiomeric separation was achieved on a chiral stationary-phase column of derivatized amylose, and the enantiomers were quantified by fluorescence detection. The method was validated for drug concns. ranging from 5 to 400 ng/mL for both enantiomers. No peaks interfering with the quantification of enantiomers were observed The limit of quantification was 5 ng/mL, with precision expressed as a coefficient of variation lower than 10.6% and accuracy expressed as relative error lower than 12.2%. The utility of this method was demonstrated by anal. of plasma samples from healthy volunteers given an oral dose of rac-E-6087. Peak plasma levels of E-6231 were higher than levels obtained for E-6232. Results were consistent with those obtained with a conventional reversed-phase method used for determination of the racemic compound

IT 251442-94-1, E-6087 251443-65-9, E-6231
251443-66-0, E-6232
RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study)
(enantioselective HPLC determination of E-6087, a new COX-2 inhibitor, in human plasma: validation and pharmacokinetic application)

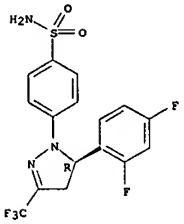
RN 251442-94-1 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 251443-65-9 CAPLUS
CN Benzenesulfonamide, 4-[(5R)-5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

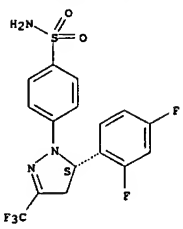
Absolute stereochemistry. Rotation (+).



RN 251443-66-0 CAPLUS
CN Benzenesulfonamide, 4-[(5S)-5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L7 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

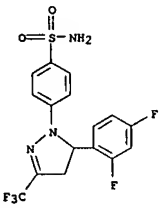
L7 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:182691 CAPLUS
DOCUMENT NUMBER: 140:210765
TITLE: Method using dialkyl ethers and other compounds for treating arthritis, cartilage damage, and other interleukin 6-mediated conditions
INVENTOR(S): Cornicelli, Joseph Anthony; Kilgore, Kenneth Stanley; Sliskovic, Drago Robert; Bove, Susan Elizabeth; Neideffer, David Herbert; Kowala, Mark Charles
PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004017952	A1	20040304	WO 2003-IB3664		20030813
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004048910	A1	20040311	US 2003-639719		20030812
CA 2494544	AA	20040304	CA 2003-2494544		20030813
EP 1539127	A1	20050615	EP 2003-792585		20030813
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003013883	A	20050719	BR 2003-13883		20030813
CN 1678297	A	20051005	CN 2003-819951		20030813
PRIORITY APPLN. INFO.:			US 2002-405250P	P	20020822
			US 2003-475443P	P	20030603
			US 2003-477092P	P	20030609
			US 2003-484808P	P	20030703
			WO 2003-IB3664	W	20030813

OTHER SOURCE(S): MARPAT 140:210765
AB The invention discloses combinations, compns., and methods using or having a substituted dialkyl ether, substituted aryl-alkyl ether, substituted dialkyl thioether, substituted dialkyl ketone, or substituted alkyl compound, or a pharmaceutically acceptable salt thereof, as an active component for preventing or treating osteoarthritis, preventing or inhibiting cartilage damage, preventing or treating rheumatoid arthritis, improving joint function, alleviating pain, including joint pain, and the like in a patient in need thereof. Compds. of the invention include e.g. 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid calcium salt (CI-1027).
IT 251442-94-1

L7 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dialkyl ethers and other compds. for treating arthritis, cartilage damage, and other interleukin 6-mediated conditions)
RN 251442-94-1 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

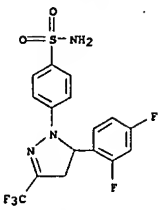
ACCESSION NUMBER: 2003:405103 CAPLUS
DOCUMENT NUMBER: 140:117541
TITLE: Determination of enantiomeric purity of a novel COX-2 anti-inflammatory drug by capillary electrophoresis using single and dual cyclodextrin systems
AUTHOR(S): Perez-Maseda, Carlos; Calvet, Carme; Cuberes, Rosa; Frigola, Jordi
CORPORATE SOURCE: Medicinal Chemistry Department, Laboratorios Dr. Esteve S.A., Barcelona, E-08041, Spain
SOURCE: Electrophoresis (2003), 24(9), 1416-1421
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English

AB E-6087 is the most advanced compound among the cyclooxygenase-2 (COX-2) inhibitor drugs developed in the authors' company. Its activity is mainly associated with the S(-)-enantiomer (E-6232), whereas the R(+)-enantiomer (E-6231) becomes an impurity whose content should be determined Five main impurities and degradation products of E-6232 were found (E-6144, E-6024, E-6072, E-6397 and E-6132), and some of them co-elute with the distomer when using a chiral high-performance liquid chromatog. (HPLC) method. Consequently, the authors have optimized the separation of all the impurities from the 2 enantiomers of E-6087 by capillary electrophoresis (CE), to use the method for the enantiomeric purity determination of E-6232. The effect of the MeOH content in the background electrolyte (BGE), the sulfobutyl ether-β-cyclodextrin (SBE-β-CD) and heptakis-(2,6-di-O-methyl)-β-cyclodextrin (DM-β-CD) concentration, and the capillary temperature were studied. Separation of all compds. could be achieved in different systems, either in a single CD-system (with SBE-β-CD) or in a dual CD-system (with DM-β-CD as a neutral CD). By using the dual CD system a limit of detection (LOD) and a limit of quantitation (LOQ) of 0.03% and 0.1% of distomer, resp., were achieved.

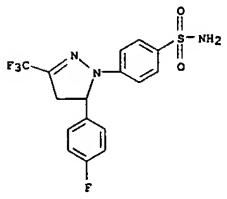
IT 251442-94-1, (±)-E 6087 251442-99-6, (±)-E 6024
251443-07-9, (±)-E 6072 251443-41-1, (±)-E 6144
251443-65-9, (R)-E 6231 251443-66-0, (S)-E 6232
RL: ANT (Analyte); ANST (Analytical study)
(determination of enantiomeric purity of a novel COX-2 anti-inflammatory drug by capillary electrophoresis using single and dual cyclodextrin systems)

RN 251442-94-1 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

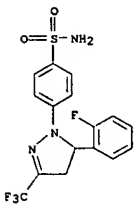


RN 251442-99-6 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

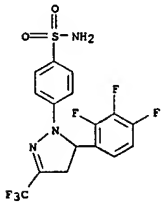


RN 251443-07-9 CAPLUS
CN Benzenesulfonamide, 4-[5-(2-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



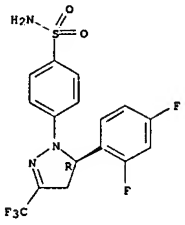
RN 251443-41-1 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-3-(trifluoromethyl)-5-(2,3,4-trifluorophenyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 251443-65-9 CAPLUS
CN Benzenesulfonamide, 4-[(5R)-5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

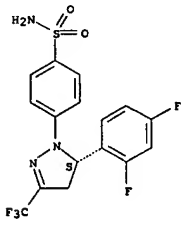
Absolute stereochemistry. Rotation (+).

L7 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 251443-66-0 CAPLUS
CN Benzenesulfonamide, 4-[(5S)-5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

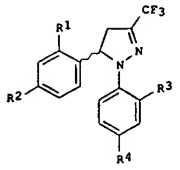
L7 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:977795 CAPLUS
DOCUMENT NUMBER: 138:55962
TITLE: Method of preparing derivatives of 1,5-diaryl-3-trifluoromethyl-Δ2-pyrazolines that are racemic and enantiomerically pure via resolution with ephedrine.
INVENTOR(S): Alcon-Marrugat, Montserrat; Pericas-Brondo, Miguel Angel; Cuberes-Altisen, Maria Rosa; Frigola-Constansa, Jordi
PATENT ASSIGNEE(S): Laboratorios Del Esteve, S.A., Spain
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102781	A1	20021227	WO 2002-ES274	20020606
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2183720	A1	20030316	ES 2001-1412	20010618
ES 2183720	B1	20040116		
CA 2451132	AA	20021227	CA 2002-2451132	20020606
EP 1408035	A1	20040414	EP 2002-735442	20020606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200400016	A	20040415	EE 2004-16	20020606
BR 2002011009	A	20041103	BR 2002-11009	20020606
JP 2005502604	T2	20050127	JP 2003-505323	20020606
US 2004019222	A1	20040129	US 2002-312194	20021217
US 6846935	B2	20050125		
BG 108524	A	20040831	BG 2004-108524	20040113
ZA 2004000343	A	20050117	ZA 2004-343	20040116
US 2005096474	A1	20050505	US 2004-6931	20041208
US 2005096373	A1	20050505	US 2004-7449	20041208
US 6958403	B2	20051025		

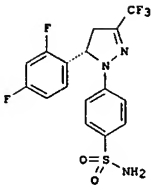
PRIORITY APPLN. INFO.:
ES 2001-1412 A 20010618
WO 2002-ES274 W 20020606
US 2002-312194 A3 20021217

OTHER SOURCE(S): CASREACT 138:55962; MARPAT 138:55962
GI

L7 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



I



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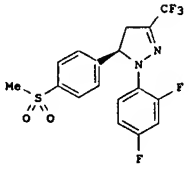
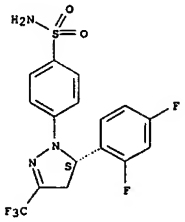


V

AB The invention relates to a method of obtaining pyrazole derivs. I, which includes racemic mixts. (±)-I and the enantiomerically pure compds. (-)-I and (+)-I [wherein: R1, R3 = H, Cl, F, Me, CF3, or OMe; R2 = H, Cl, F, Me, CF3, OMe, OCF3, SO2Me, or SO2NH2; R4 = H, Cl, F, Me, CF3, OMe, OCF3, SO2Me, or SO2NH2; provided that one of R2 or R4 = SO2Me or SO2NH2]. I are cyclooxygenase-2 inhibitors, useful as antiinflammatories, which are known from WO 9962884. The method allows use of economical (un)substituted benzaldehydes and phenylhydrazines, instead of more expensive 4-methylsulfonyl- and 4-aminosulfonyl-substituted compds. The method involves production of racemic (±)-I by reaction of an (E)-1,1,1-trifluoro-4-aryl-3-butene-2-one with a phenylhydrazine, followed by treatment with chlorosulfonic acid, or by reaction with chlorosulfonic acid followed by reaction with sodium hydroxide and, finally, with thionyl chloride. The product obtained by any of the aforementioned methods (i.e., the sulfonyl chloride) then reacts with ammonium carbonate or ammonia, or with sodium sulfite and then Me iodide or di-Me sulfate. To produce enantiomerically pure I via resolution of (±)-I, the resolution is carried out with optically active ephedrine, followed by formation of the

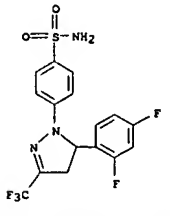
L7 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
sodium salt of each of the enantiomers, reaction of these with (a) thionyl chloride and then ammonia or ammonium carbonate, or (b) with thionyl chloride followed by sodium sulfite and then Me iodide or di-Me sulfate, giving (+)- and (-)-I. For instance, (S)-(-)-II was prepd. in 5 steps, by: (1) cyclocondensation of (E)-1,1,1-trifluoro-4-(2,4-difluorophenyl)-3-buten-2-one with PhNHNH2.HCl in the presence of p-MeC6H4SO3H.H2O to give (±)-1-phenyl-5-(2,4-difluorophenyl)-4,5-dihydro-3-trifluoromethyl-1H-pyrazole in 65% yield; (2) chlorosulfonation of the latter with ClSO3H and hydrolysis with NaOH to give (±)-Na 4-[5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]-benzenesulfonate [(±)-III.Na] in 75% yield; (3) resoln. of the latter with (+)-ephedrine-HCl [(+)-IV.HCl] in CHCl3 to give (-)-III.(+)-IV salt with >98% enantiomeric excess (ee); (4) treatment of the salt with NaCl and NaOH in iso-PrOH to give (-)-III.Na; and (5) treatment of this with SOCl2, and then (NH4)2CO3, to give (S)-(-)-II in 84% yield and >99% ee after recrystn. The invention sulfone (R)-(-)-V was similarly prepd., using the other method variant with Na2SO3 and MeI.
IT 251443-66-0P, (S)-(-)-4-[5-(2,4-Difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(target compound; improved, economical preparation of diaryl(trifluoromethyl)pyrazoline enantiomers from benzaldehydes and phenylhydrazines via ephedrine resolution)
RN 251443-66-0 CAPLUS
CN Benzenesulfonamide, 4-[(5S)-5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

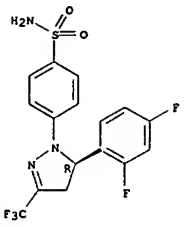
L7 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:856309 CAPLUS
DOCUMENT NUMBER: 139:17018
TITLE: Enantioseparation of novel COX-2 anti-inflammatory drugs by capillary electrophoresis
AUTHOR(S): Perez-Maseda, C.; Calvet, C.; Cuberes, R.; Frigola, J.
CORPORATE SOURCE: Medicinal Chemistry Department, Laboratorios Dr. Esteve S.A., Barcelona, E-08041, Spain
SOURCE: Bioforum International (2002), 6(5), 275-277
CODEN: BINTFQ; ISSN: 1434-2693
PUBLISHER: GIT Verlag GmbH & Co. KG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A capillary electrophoresis (CE) method was developed for the enantiosepn. of three novel COX-2 inhibitor drugs (E-6259, E-6036 and E-6087) with anti-inflammatory and analgesic activities using sulfobutylether-β-cyclodextrin (SBE-β-CD) as a chiral selector. The use of 50 mM sodium tetraborate at pH 9.2, 7.1 mM SBE-β-CD and 30 % MeOH (volume/volume), as a background electrolyte (BGE), allowed the complete enantiosepn. of the three neutral racemates and their corresponding metabolites in a single run. Migration times were shortened by adding 1.75 mM dimethyl-β-cyclodextrin (DM-β-CD) to the previous BGE (dual CD system). The reversal of the migration order of E-6259 enantiomers in the dual CD system was also studied.
IT 251442-94-1P, (±)-E 6087 251443-65-9P, (R)-E 6232
251443-66-0P, (S)-E 6232
RL: ANT (Analyte); PUR (Purification or recovery); ANST (Analytical study); PREP (Preparation)
(enantiosepn. of novel COX-2 anti-inflammatory drugs by capillary electrophoresis)
RN 251442-94-1 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 251443-65-9 CAPLUS
CN Benzenesulfonamide, 4-[(5R)-5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

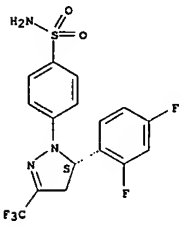
Absolute stereochemistry. Rotation (+).

L7 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 251443-66-0 CAPLUS
CN Benzenesulfonamide, 4-[(5S)-5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:793411 CAPLUS
DOCUMENT NUMBER: 137:310911
TITLE: Utilization of pyrazoline derivatives, as inhibitors of the expression of the gene responsible for COX-2 synthesis, in the preparation of a medicament for the prevention and/or treatment of proliferative cell diseases
INVENTOR(S): Cuberes-Altisent, Maria Rosa; Berrocal-Romero, Juana Maria; Contijoch-Llobet, Maria Montserrat; Frigola-Constansa, Jordi
PATENT ASSIGNEE(S): Laboratorios del Esteve, S.A., Spain
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080909	A1	20021017	WO 2002-ES137	20020321
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2174757	A1	20021101	ES 2001-818	20010406
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CA 2442974	AA	20021017	CA 2002-2442974	20020321
EP 1384477	A1	20040128	EP 2002-714233	20020321
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CN 1509171	A	20040630	CN 2002-809893	20020321
BR 2002008805	A	20040713	BR 2002-8805	20020321
JP 2004525166	T2	20040819	JP 2002-578948	20020321
ZA 2003008626	A	20041105	ZA 2003-8626	20020321
EP 1516621	A2	20050323	EP 2004-30751	20020321
EP 1516621	A3	20050504		
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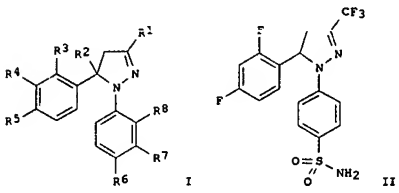
US 2004034082	A1	20040219	US 2002-312193	20021217
NO 2003004470	A	20031205	NO 2003-4470	20031006

PRIORITY APPLN. INFO.:
ES 2001-818 A 20010406
EP 2002-714233 A3 20020321
WO 2002-ES137 W 20020321

OTHER SOURCE(S): MARPAT 137:310911
GI

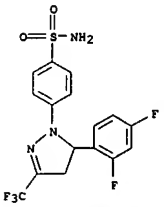
L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



AB The invention relates to pyrazoline derivs. I [wherein R1 = H, Me, CH2F, CHF2, CF3, CO2H, C1-4 alkoxycarbonyl, CONH2, or cyano; R2 = H or Me; R3, R4, R7, R8 = H, Cl, F, Me, CF3, or OMe; R5, R6 = H, Cl, F, Me, CF3, OMe, OCF3, SO2Me, SO2NH2, or SO2NHAc, provided that 1 of R5 or R6 = SO2Me, SO2NH2, or SO2NHAc, and provided that if R1 = Me, then: R2 = H or Me; R3 and R8 = H, Cl, F, Me, or CF3; R4 = H, F, Me, CF3, or OMe; R5 = F, CF3, CF3O, SO2Me, SO2NH2, or SO2NHAc; R6 = H, Cl, F, Me, CF3, OMe, OCF3, SO2Me, SO2NH2, or SO2NHAc, provided that 1 of the substituents R5 or R6 = SO2Me, SO2NH2, or SO2NHAc; and R7 = H, Cl, F, Me, CF3, or OMe; including physiol. acceptable salts]. I are useful for the prevention or treatment of proliferative cell diseases. In particular, I are useful for treatment of pre-neoplastic or neoplastic processes, tumoral angiogenesis, cachexia, and processes related to tumor necrosis factor (TNF). Generally, I are useful for treating processes where there would be benefit by inhibiting the expression of the gene responsible for the synthesis of cyclooxygenase 2 (COX-2), notably in mammals, and particularly in humans. A list of 84 specific examples is provided, and a similar list of 84 compds. (1 difference) is claimed. Six examples of individual enantiomers are given, the remainder being racemic. For instance, condensation of 2,4-difluorobenzaldehyde with either CH3COCF3 (68%) or the reaction product of LiCH2PO3Et2 with PhN:C(Cl)CF3 (81%) gave (E)-1,1,1-trifluoro-4-(2,4-difluorophenyl)-3-buten-2-one. Cyclocondensation of the latter enone with 4-(H2NSO2)C6H4NHNH2.HCl gave 61% invention compound (±)-II, which was resolved by chromatog. on CHIRALPAK AS to give (+)- and (-)-II with enantiomeric purities of 99.9% or greater. In tests against human colorectal cancer cell lines HC59 and TD20, (±)-II had IC50 values of 29.87 and 33.87 μM, resp. I also inhibited the induction of COX-2 in JURKAT cells, were active against breast cancer cells in culture (IC50 12-18 μM), inhibited angiogenesis (as determined by induction of expression of VEGF and TF in cell culture), and inhibited production of TNF-α in the air-pouch model in mice.

IT 251442-94-1P, 1-(4-Aminosulfonylphenyl)-5-(2,4-difluorophenyl)-4,5-dihydro-3-trifluoromethyl-1H-pyrazole

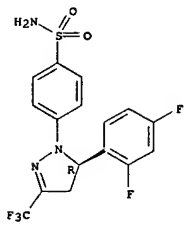
L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(drug candidate, resoln.; prepn. and use of pyrazoline derivs. as COX-2 gene expression inhibitors for prevention and/or treatment of proliferative cell diseases)
RN 251442-94-1 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



IT 251443-65-9P, (+)-1-(4-Aminosulfonylphenyl)-5-(2,4-difluorophenyl)-4,5-dihydro-3-trifluoromethyl-1H-pyrazole 251443-66-0P, (-)-1-(4-Aminosulfonylphenyl)-5-(2,4-difluorophenyl)-4,5-dihydro-3-trifluoromethyl-1H-pyrazole
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation and use of pyrazoline derivs. as COX-2 gene expression inhibitors for prevention and/or treatment of proliferative cell diseases)
RN 251443-65-9 CAPLUS
CN Benzenesulfonamide, 4-[(5R)-5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

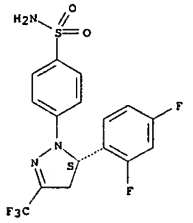
Absolute stereochemistry. Rotation (+).

L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 251443-66-0 CAPLUS
CN Benzenesulfonamide, 4-[(5S)-5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 251442-92-9P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(4-methylphenyl)-3-trifluoromethyl-1H-pyrazole 251442-93-0P,

1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-methyl-5-phenyl-3-trifluoromethyl-1H-pyrazole 251442-96-3P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-phenyl-3-trifluoromethyl-1H-pyrazole 251442-99-6P,

1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(4-fluorophenyl)-3-trifluoromethyl-1H-pyrazole 251443-02-4P, 1-(4-Aminosulfonylphenyl)-5-(3,4-difluorophenyl)-4,5-dihydro-3-trifluoromethyl-1H-pyrazole 251443-04-6P, 1-(4-Aminosulfonylphenyl)-5-(2,4-dichlorophenyl)-4,5-dihydro-3-trifluoromethyl-1H-pyrazole 251443-05-7P,

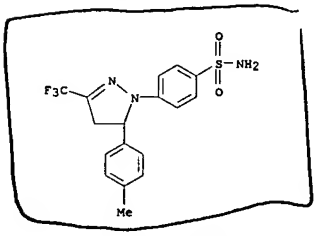
L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(2-methylphenyl)-3-trifluoromethyl-1H-pyrazole 251443-06-8P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(3-methylphenyl)-3-trifluoromethyl-1H-pyrazole 251443-07-9P,

1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(2-fluorophenyl)-3-trifluoromethyl-1H-pyrazole 251443-09-1P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(3-fluorophenyl)-3-trifluoromethyl-1H-pyrazole 251443-11-5P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(4-methoxyphenyl)-3-trifluoromethyl-1H-pyrazole 251443-12-6P, 1-(4-Aminosulfonylphenyl)-5-(3-chloro-4-fluorophenyl)-4,5-dihydro-3-trifluoromethyl-1H-pyrazole 251443-13-7P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-3-trifluoromethyl-5-(4-trifluoromethoxyphenyl)-1H-pyrazole 251443-14-8P, 1-(4-Aminosulfonylphenyl)-5-(2,3-difluorophenyl)-4,5-dihydro-3-trifluoromethyl-1H-pyrazole 251443-15-9P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(2,4-dimethylphenyl)-3-trifluoromethyl-1H-pyrazole 251443-34-2P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(3,4-dimethylphenyl)-3-trifluoromethyl-1H-pyrazole 251443-35-3P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(3-methyl-4-methoxyphenyl)-3-trifluoromethyl-1H-pyrazole 251443-36-4P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(3-fluoro-4-methoxyphenyl)-3-trifluoromethyl-1H-pyrazole 251443-37-5P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(2-fluoro-4-methoxyphenyl)-3-trifluoromethyl-1H-pyrazole 251443-38-6P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(2,4-dimethoxyphenyl)-3-trifluoromethyl-1H-pyrazole 251443-39-7P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(4-fluoro-2-methoxyphenyl)-3-trifluoromethyl-1H-pyrazole 251443-41-1P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(2,3,4-trifluorophenyl)-3-trifluoromethyl-1H-pyrazole 251443-42-2P, 1-(4-Aminosulfonylphenyl)-5-(2-chloro-4-fluorophenyl)-4,5-dihydro-3-trifluoromethyl-1H-pyrazole 251443-43-3P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(2-fluoro-4-trifluoromethylphenyl)-3-trifluoromethyl-1H-pyrazole 251443-44-4P, 1-(4-Aminosulfonylphenyl)-5-[2,4-bis(trifluoromethyl)phenyl]-4,5-dihydro-3-trifluoromethyl-1H-pyrazole 251443-45-5P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(2-methyl-3-fluorophenyl)-3-trifluoromethyl-1H-pyrazole 251443-46-6P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(2-methyl-4-methoxyphenyl)-3-trifluoromethyl-1H-pyrazole 251443-48-8P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(4-fluoro-2-trifluoromethylphenyl)-3-trifluoromethyl-1H-pyrazole 251443-50-2P, 1-(4-Aminosulfonylphenyl)-5-(2-chlorophenyl)-4,5-dihydro-3-trifluoromethyl-1H-pyrazole 251443-51-3P, 1-(4-Aminosulfonylphenyl)-5-(4-chloro-2-fluorophenyl)-4,5-dihydro-3-trifluoromethyl-1H-pyrazole 251443-52-4P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(4-fluoro-2-methylphenyl)-3-trifluoromethyl-1H-pyrazole 251443-53-5P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-(2-fluoro-4-methylphenyl)-3-trifluoromethyl-1H-pyrazole 251443-54-6P, 1-(4-Acetylaminosulfonylphenyl)-5-(2,4-difluorophenyl)-4,5-dihydro-3-trifluoromethyl-1H-pyrazole 471646-23-8P, 1-(4-Aminosulfonylphenyl)-4,5-dihydro-5-methyl-5-(4-methylphenyl)-3-trifluoromethyl-1H-pyrazole

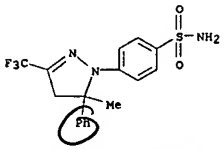
L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. and use of pyrazoline derivs. as COX-2 gene expression inhibitors for prevention and/or treatment of proliferative cell diseases)

RN 251442-92-9 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



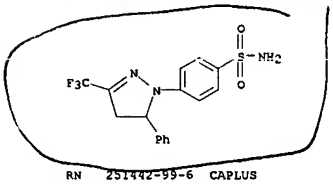
H for Me, Position

RN 251442-93-0 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-methyl-5-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



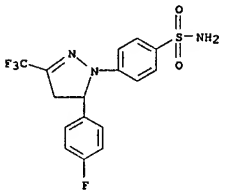
RN 251442-96-3 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

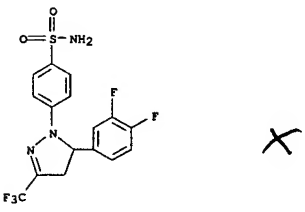


2 H for Me

RN 251442-99-6 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

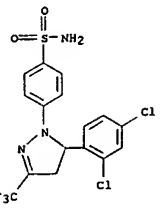


RN 251443-02-4 CAPLUS
CN Benzenesulfonamide, 4-[5-(3,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

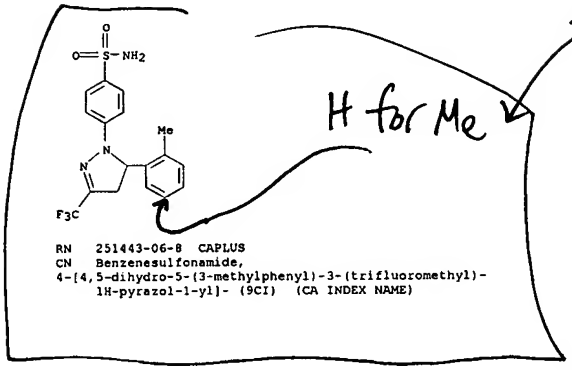


RN 251443-04-6 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dichlorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

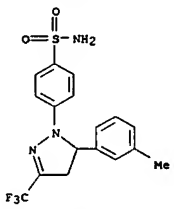


RN 251443-05-7 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-(2-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

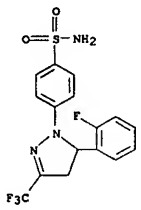


RN 251443-06-8 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-(3-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

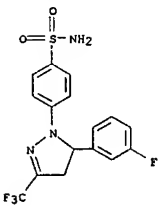


RN 251443-07-9 CAPLUS
CN Benzenesulfonamide, 4-[5-(2-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

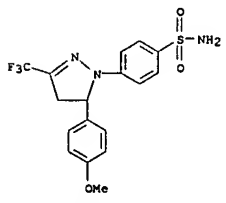


RN 251443-09-1 CAPLUS
CN Benzenesulfonamide, 4-[5-(3-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

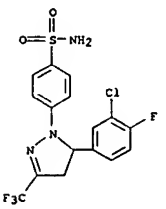
L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 251443-11-5 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-(4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

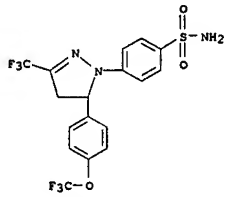


RN 251443-12-6 CAPLUS
CN Benzenesulfonamide, 4-[5-(3-chloro-4-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

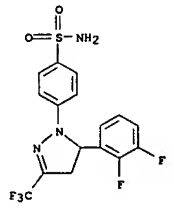


L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 251443-13-7 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-[4-(trifluoromethoxy)phenyl]-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

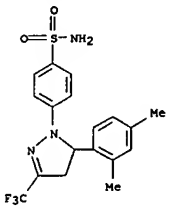


RN 251443-14-8 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,3-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



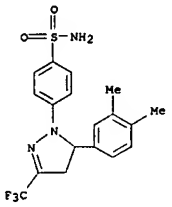
RN 251443-15-9 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dimethylphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



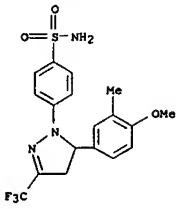
positional

RN 251443-34-2 CAPLUS
CN Benzenesulfonamide, 4-[5-(3,4-dimethylphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

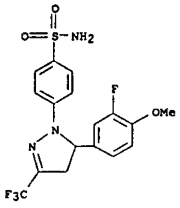


RN 251443-35-3 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-(4-methoxy-3-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

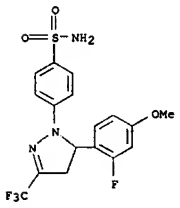


RN 251443-36-4 CAPLUS
CN Benzenesulfonamide, 4-[5-(3-fluoro-4-methoxyphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

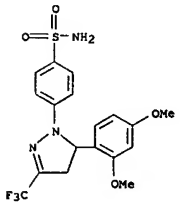


RN 251443-37-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2-fluoro-4-methoxyphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

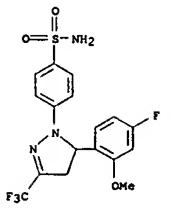
L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 251443-38-6 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dimethoxyphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

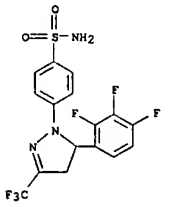


RN 251443-39-7 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-fluoro-2-methoxyphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

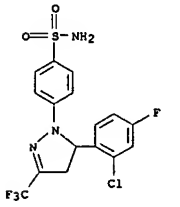


L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 251443-41-1 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-3-(trifluoromethyl)-5-(2,3,4-trifluorophenyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

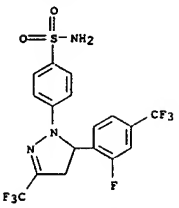


RN 251443-42-2 CAPLUS
CN Benzenesulfonamide, 4-[5-(2-chloro-4-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

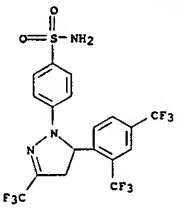


RN 251443-43-3 CAPLUS
CN Benzenesulfonamide, 4-[5-[2-fluoro-4-(trifluoromethyl)phenyl]-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

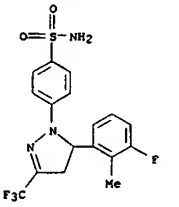


RN 251443-44-4 CAPLUS
CN Benzenesulfonamide, 4-[5-[2,4-bis(trifluoromethyl)phenyl]-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

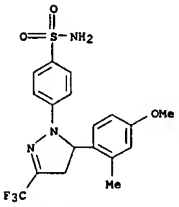


RN 251443-45-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(3-fluoro-2-methylphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

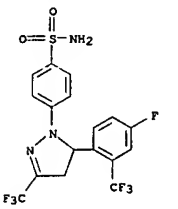


RN 251443-46-6 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-(4-methoxy-2-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

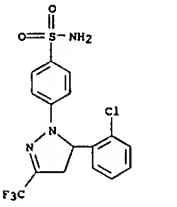


RN 251443-48-8 CAPLUS
CN Benzenesulfonamide, 4-[5-[4-fluoro-2-(trifluoromethyl)phenyl]-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

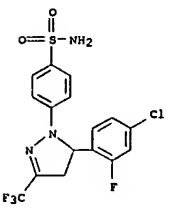
L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 251443-50-2 CAPLUS
CN Benzenesulfonamide, 4-[5-(2-chlorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

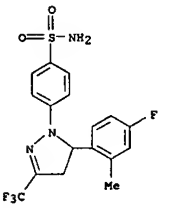


RN 251443-51-3 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chloro-2-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

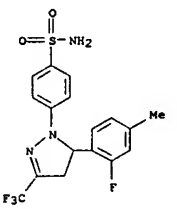


L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 251443-52-4 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-fluoro-2-methylphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

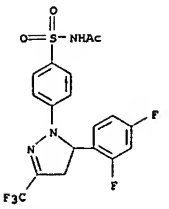


RN 251443-53-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2-fluoro-4-methylphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

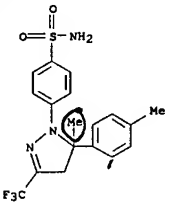


RN 251443-54-6 CAPLUS
CN Acetamide, N-[[4-[5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



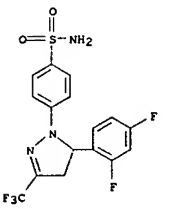
RN 471646-23-8 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-methyl-5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

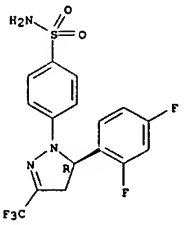
L7 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:505977 CAPLUS
DOCUMENT NUMBER: 137:375361
TITLE: Enantioseparation of novel COX-2 anti-inflammatory drugs by capillary electrophoresis using single and dual cyclodextrin systems
AUTHOR(S): Calvet, Carmen; Cuberes, Rosa; Perez-Maseda, Carlos; Frigola, Jordi
CORPORATE SOURCE: Medicinal Chemistry Department, Laboratorios Dr. Esteve S. A., Barcelona, E-08041, Spain
SOURCE: Electrophoresis (2002), 23(11), 1702-1708
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A capillary electrophoresis method was developed for the enantiosepn. of three novel cyclooxygenase-2 (COX-2) inhibitor drugs (E-6259, E-6036 and E-6087) with anti-inflammatory and analgesic activities using sulfobutyl ether-β-cyclodextrin (SBE-β-CD) as a chiral selector. The use of 50 mM sodium tetraborate at pH 9.2 with 30% volume/volume methanol, containing 7.1 mM SBE-β-CD, as a background electrolyte (BGE) allowed the complete enantiosepn. of the three neutral racemic mixts. (resolution = 2.4, 3.0 and 8.7, resp.) and their corresponding metabolites (oxidation products) in a single run. Migration times were shortened with some loss of enantioresoln. by adding 1.75 mM dimethyl-β-cyclodextrin (DM-β-CD) to the previous BGE (dual CD system). The reversal of the migration order of E-6259 enantiomers in the dual CD system was also studied. Furthermore, the addition of DM-β-CD to the BGE introduced a new chemoselectivity in the system that allowed E-6259 to be separated from the structurally similar compound E-6036.
IT 251442-94-1 251443-65-9 251443-66-0
RL: ANT (Analyte); ANST (Analytical study)
(enantiosepn. of novel COX-2 anti-inflammatory drugs by capillary electrophoresis using single and dual cyclodextrin systems)
RN 251442-94-1 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 251443-65-9 CAPLUS
CN Benzenesulfonamide, 4-[(5R)-5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

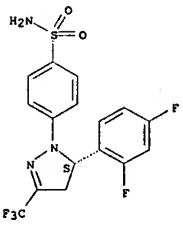
Absolute stereochemistry. Rotation (+).



RN 251443-66-0 CAPLUS
CN Benzenesulfonamide, 4-[(5S)-5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

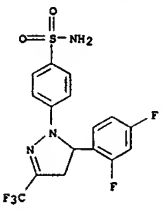
L7 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:78060 CAPLUS
DOCUMENT NUMBER: 136:318794
TITLE: Pharmacokinetics of E-6087, a new anti-inflammatory agent, in rats and dogs
AUTHOR(S): Reinoso, Raquel F.; Farran, Ramon; Moragon, Trinidad; Garcia-Soret, Antonio; Martinez, Lluis
CORPORATE SOURCE: Department of Pharmacokinetics and Drug Metabolism, Laboratorios Dr. Esteve S.A., Barcelona, 08041, Spain
SOURCE: Biopharmaceutics & Drug Disposition (2001), 22(6), 231-242
CODEN: BDDID8; ISSN: 0142-2782
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pharmacokinetics of E-6087, a newly developed cyclooxygenase-2 inhibitor, was studied in rats and dogs after single oral and i.v. doses. In both animal species, E-6087 was characterized by a long elimination half-life (20-35 h), a low plasma clearance (0.10-0.22 l h-1 kg-1) and a relatively large volume of distribution (2-6 l kg-1). Oral bioavailability was lower in dogs than in rats whereas a faster elimination was found in rats. Multiple peaks were present regardless of administration route and animal species, suggesting the existence of enterohepatic circulation. Gender effect on the pharmacokinetics of E-6087 was only found in rats, with greater exposure and longer elimination in females than in males. Food intake reduced the bioavailability (22%) with no apparent changes in the absorption rate. After oral dosing of 1, 5 and 25 mg kg-1 to rats, linearity was lost at the highest dose due to the low aqueous solubility of E-6087. Drug absorption was improved by micronization. E-6087 and E-6132, (a pharmacol. active metabolite), showed different pharmacokinetics. The higher percentage of E-6087 at early times suggests that E-6087 is the main compound responsible for in vivo activity, although E-6132 would contribute to the activity at later times.
IT 251442-94-1, E 6087
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetics of E-6087 in rats and dogs)
RN 251442-94-1 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

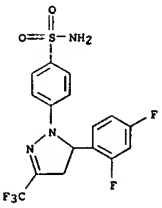
L7 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:182563 CAPLUS
DOCUMENT NUMBER: 135:70541
TITLE: Development and validation of two chromatographic methods for the quantification of E-6087 and one of its metabolites, E-6132, in rat plasma
AUTHOR(S): Reinoso, R. F.; Farran, R.; Moragon, T.; Garcia-Soret, A.; Martinez, L.
CORPORATE SOURCE: Department of Pharmacokinetics and Drug Metabolism, Laboratorios Dr Esteve, Barcelona, S.A., 08041, Spain
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2001), 24(5-6), 897-911
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB E-6087 is a nonsteroidal anti-inflammatory compound under development that selectively inhibits cyclooxygenase-2. In vitro studies have shown that one of its metabolites, E-6132, also inhibits this enzyme. Due to chromatog. reasons, two reverse phase HPLC methods were developed and validated in order to elucidate which compound is responsible for the pharmacol. activity in vivo. Chromatog. separation of E-6087 was achieved using acetonitrile-phosphate buffer (pH 2.5; 25 mM) (60:40, volume/volume) as mobile phase and two 4.6+150 mm+5 μm Inertsil ODS-2 columns. For E-6132, two Inertsil ODS-3 columns and 52% of acetonitrile were used instead. Internal stds. and fluorescence detection differed between both methods. The same online solid-phase extraction method was used. Mean retention times for E-6087 and E-6132 were 15.2 (±1.3) and 36.1 (±0.6) min, resp. The methods were selective and linear over the concentration range of 10-500 ng ml-1 (r2>0.996) for E-6087 and 5-200 ng ml-1 (r2>0.997) for E-6132. The limits of quantitation were 10 ng ml-1 (E-6087) and 5 ng ml-1 (E-6132) with a precision and accuracy <16% (E-6087) and <11% (E-6132). Mean recoveries from plasma were 43.2-61.9% (E-6087) and 60.4-65.2% (E-6132). For both compds., both inter-assay and intra-assay precision and accuracy were within acceptable limits (<15%). As an example of the suitability of these methods, the results from a pharmacokinetic study are reported. After single oral administration of 5 mg kg-1 of E-6087 to rats, plasma concns. of E-6087 at peak time were higher than those of E-6132, suggesting that activity is mainly due to E-6087.
IT 251442-94-1
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(development and validation of two chromatog. methods for quantification of E-6087 and its metabolite, E-6132, in rat plasma)
RN 251442-94-1 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



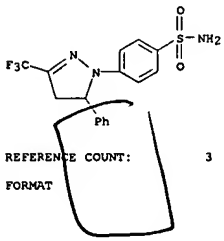
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:900446 CAPLUS
DOCUMENT NUMBER: 134:42125
TITLE: 1-(4-Sulfamylaryl)-3-substituted-5-aryl-2-pyrazolines, method of preparation and use as inhibitors of cyclooxygenase-2
INVENTOR(S): Reddy, E. Premkumar; Reddy, M. V. Ramana
PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of Higher Education, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076503	A1	20001221	WO 2000-US16656	20000616
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2377153	AA	20001221	CA 2000-2377153	20000616
EP 1191931	A1	20020403	EP 2000-939946	20000616
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6376519	B1	20020423	US 2000-595760	20000616
JP 2003501464	T2	20030114	JP 2001-502836	20000616
NZ 516553	A	20040130	NZ 2000-516553	20000616
AU 771668	B2	20040401	AU 2000-54951	20000616
PRIORITY APPLN. INFO.:			US 1999-139416P P	19990616
			WO 2000-US16656 W	20000616

OTHER SOURCE(S): MARPAT 134:42125
AB 1-(4-Sulfamylaryl)-3-X-5-Z-2-pyrazolines (X = trihalomethyl, C1-C6 alkyl, and C6H3R3R4 (R3, R4 = H, halogen, hydroxyl, nitro, C1-C6 alkyl, C1-C6 alkoxy, carboxy, C1-C6 trihaloalkyl, CN); Z = substituted and unsubstituted aryl) or a pharmaceutically acceptable salt thereof, a method of preparation and uses as inhibitors of cyclooxygenase-2 activity are claimed. They are useful for treating cyclooxygenase-mediated disorders, including, for example, inflammation, neoplastic disorders and angiogenesis-mediated disorders. The compds. of the invention preferably are characterized by a selectivity ratio for cyclooxygenase-2 inhibition over cyclooxygenase-1 inhibition of at least .apprx.50, more preferably at least .apprx.100; data are reported for 1-(4-sulfamylphenyl)-3-trifluoromethyl-5-phenyl-2-pyrazoline and 1-(4-sulfamylphenyl)-3-

L7 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
trifluoromethyl-5-(3-indolyl)-2-pyrazoline. The claimed method of prepn. comprises reacting trans-2CH:CHC(O)X with 4-sulfamylphenylhydrazine or salt thereof.
IT 251442-96-3P, 1-(4-Sulfamylphenyl)-3-trifluoromethyl-5-phenyl-2-pyrazoline
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-(4-sulfamylaryl)-3-substituted-5-aryl-2-pyrazolines useful as selective inhibitors of cyclooxygenase-2)
RN 251442-96-3 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



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1H for Me

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

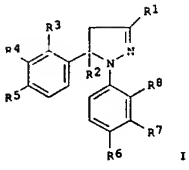
X

L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:784081 CAPLUS
DOCUMENT NUMBER: 132:12302
TITLE: Diarylpyrazoles as inhibitors of cyclooxygenase-2
INVENTOR(S): Cuberes-Altisent, Maria Rosa; Berrocal-Romero, Juana Maria; Contijoch-Llobet, Maria Montserrat; Frigola-Constansa, Jordi
PATENT ASSIGNEE(S): Laboratorios Del Esteve, S.A., Spain
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962884	A1	19991209	WO 1999-ES156	19990527
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ES 2137138	A1	19991201	ES 1998-1129	19980529
ES 2137138	B1	20000916		
CA 2333475	AA	19991209	CA 1999-2333475	19990527
AU 9939329	A1	19991220	AU 1999-39329	19990527
AU 752001	B2	20020905		
EP 1083171	A1	20010314	EP 1999-922192	19990527
EP 1083171	B1	20040428		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9910801	A	20011127	BR 1999-10801	19990527
SI 20580	C	20011231	SI 1999-20042	19990527
JP 2002516908	T2	20020611	JP 2000-552096	19990527
NZ 508990	A	20021220	NZ 1999-508990	19990527
TW 572898	B	20040121	TW 1999-88108709	19990527
AT 265437	E	20040515	AT 1999-922192	19990527
RU 2233272	C2	20040727	RU 2000-133231	19990527
PT 1083171	T	20040930	PT 1999-922192	19990527
ES 2221382	T3	20041216	ES 1999-922192	19990527
NO 2000006029	A	20010126	NO 2000-6029	20001128
LT 4879	B	20020125	LT 2000-108	20001128
US 6353117	B1	20020305	US 2000-701276	20001128
BG 105005	A	20010831	BG 2000-105005	20001129
ZA 2000007638	A	20011113	ZA 2000-7638	20001219
LV 12632	B	20010720	LV 2000-161	20001228
PRIORITY APPLN. INFO.:			ES 1998-1129 A	19980529
			WO 1999-ES156 W	19990527

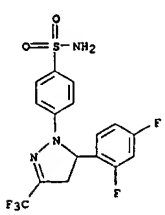
OTHER SOURCE(S): MARPAT 132:12302
GI

L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



I

AB Diarylpyrazoles I [R1 = H, Me, CH2F, CHF2, CF3, CO2H, alkoxycarbonyl, carbamoyl, CN; R2 = H, Me; R3, R4, R7, R8 = H, Cl, F, Me, CF3, OMe; R5 = H, Cl, F, Me, CF3, OMe, OCF3, R6 = SO2Me, SO2NH2, SO2NHAc; R5 = SO2Me, SO2NH2, SO2NHAc, R6 = H, Cl, F, Me, CF3, OMe, OCF3] were prepared for use in treating inflammation and other processes mediated by COX-2. Thus, 2,4-F2C6H3CHO was treated with CF3COMe to give (E)-2,4-F2C6H3CH:CHCOCF3 which was cyclized with 4-H2NSO2C6H4NHNH2 to give I [R1 = CF3, R2-R4, R7, R8 = H, R5 = SO2Me, R6 = Me] which gave 92% inhibition of COX-2 activity at 40 mg/kg orally in rats.
IT 251442-94-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of diarylpyrazoles as inhibitors of cyclooxygenase-2)
RN 251442-94-1 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

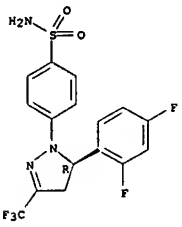


X

IT 251443-65-9P 251443-66-0P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diarylpyrazoles as inhibitors of cyclooxygenase-2)
RN 251443-65-9 CAPLUS

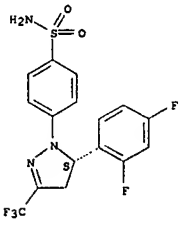
L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN Benzenesulfonamide, 4-[(5R)-5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



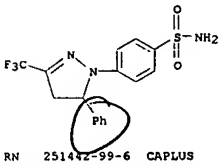
RN 251443-66-0 CAPLUS
CN Benzenesulfonamide, 4-[(5S)-5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

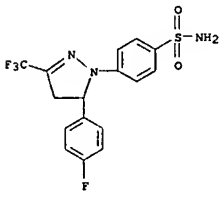


IT 251442-92-9P 251442-93-0P 251442-96-3P
251442-99-6P 251443-02-4P 251443-04-6P
251443-05-7P 251443-06-8P 251443-07-9P
251443-09-1P 251443-11-5P 251443-12-6P
251443-13-7P 251443-14-8P 251443-15-9P
251443-34-2P 251443-35-3P 251443-36-4P
251443-37-5P 251443-38-6P 251443-39-7P
251443-41-1P 251443-42-2P 251443-43-3P

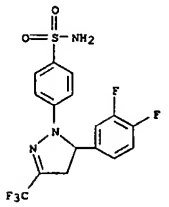
L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 251442-99-6 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

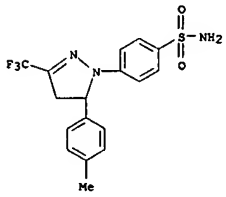


RN 251443-02-4 CAPLUS
CN Benzenesulfonamide, 4-[5-(3,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

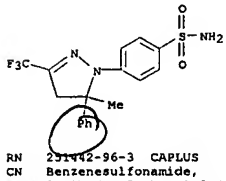


RN 251443-04-6 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dichlorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
251443-44-4P 251443-45-5P 251443-46-6P
251443-48-8P 251443-50-2P 251443-51-3P
251443-52-4P 251443-53-5P 251443-54-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diarylpyrazoles as inhibitors of cyclooxygenase-2)
RN 251442-92-9 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

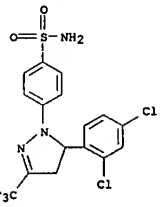


RN 251442-93-0 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-methyl-5-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

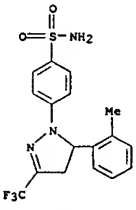


RN 251442-96-3 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



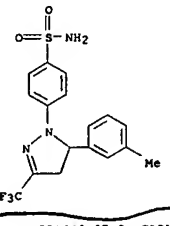
RN 251443-05-7 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-(2-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



H for Me ?

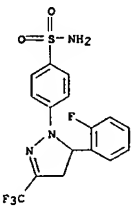
RN 251443-06-8 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-(3-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



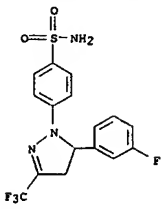
H for Me

RN 251443-07-9 CAPLUS
CN Benzenesulfonamide, 4-[5-(2-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

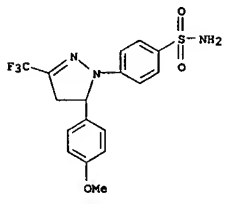


RN 251443-09-1 CAPLUS
CN Benzenesulfonamide, 4-[5-(3-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

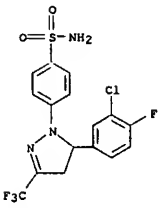


RN 251443-11-5 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-(4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

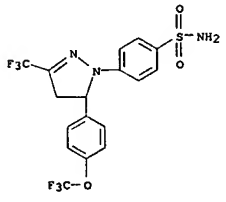


RN 251443-12-6 CAPLUS
CN Benzenesulfonamide, 4-[5-(3-chloro-4-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

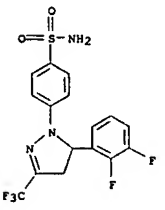
L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 251443-13-7 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-[4-(trifluoromethoxy)phenyl]-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

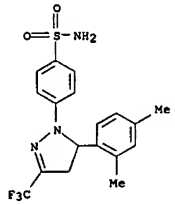


RN 251443-14-8 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,3-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



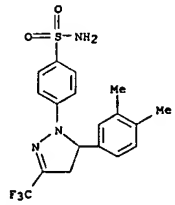
L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 251443-15-9 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dimethylphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



positional isomers

RN 251443-34-2 CAPLUS
CN Benzenesulfonamide, 4-[5-(3,4-dimethylphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



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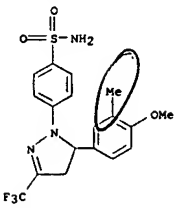
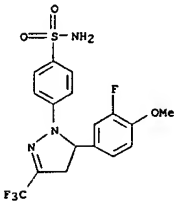
RN 251443-35-3 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-(4-methoxy-3-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

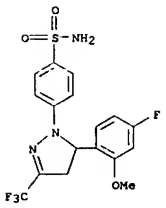


RN 251443-36-4 CAPLUS
CN Benzenesulfonamide, 4-[5-(3-fluoro-4-methoxyphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

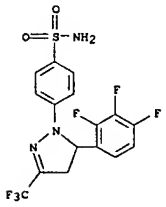


RN 251443-37-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2-fluoro-4-methoxyphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

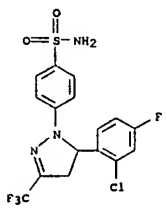
L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



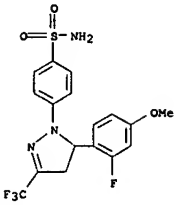
RN 251443-41-1 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-3-(trifluoromethyl)-5-(2,3,4-trifluorophenyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



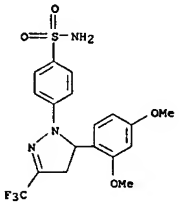
RN 251443-42-2 CAPLUS
CN Benzenesulfonamide, 4-[5-(2-chloro-4-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



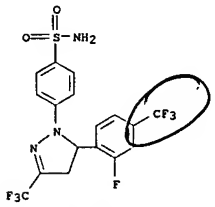
RN 251443-38-6 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dimethoxyphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



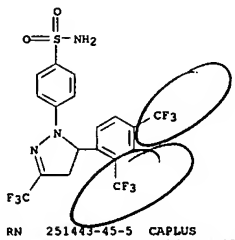
RN 251443-39-7 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-fluoro-2-methoxyphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 251443-43-3 CAPLUS
CN Benzenesulfonamide, 4-[5-[2-fluoro-4-(trifluoromethyl)phenyl]-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 251443-44-4 CAPLUS
CN Benzenesulfonamide, 4-[5-[2,4-bis(trifluoromethyl)phenyl]-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



positional

RN 251443-45-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(3-fluoro-2-methylphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

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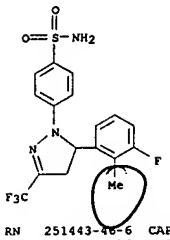
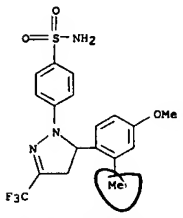
L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

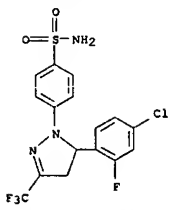


RN 251443-46-6 CAPLUS
CN Benzenesulfonamide, 4-[4,5-dihydro-5-(4-methoxy-2-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

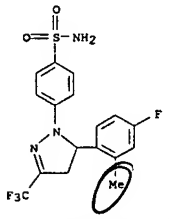


RN 251443-48-8 CAPLUS
CN Benzenesulfonamide, 4-[5-[4-fluoro-2-(trifluoromethyl)phenyl]-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

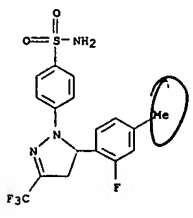
L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



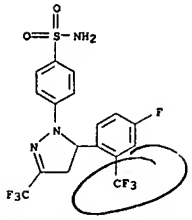
RN 251443-52-4 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-fluoro-2-methylphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



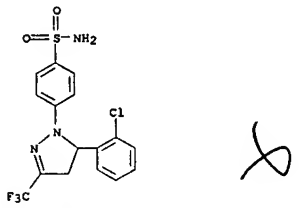
RN 251443-53-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2-fluoro-4-methylphenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



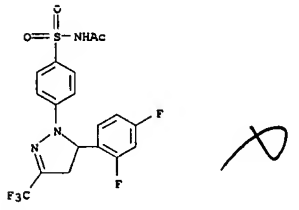
RN 251443-50-2 CAPLUS
CN Benzenesulfonamide, 4-[5-(2-chlorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 251443-51-3 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chloro-2-fluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 251443-54-6 CAPLUS
CN Acetamide, N-[[4-[5-(2,4-difluorophenyl)-4,5-dihydro-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



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